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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/955,367	09/18/2001	Alan D. Attic	960296.97478	8344

7590 07/31/2007

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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	**PAPER NUMBER**
1634	
MAIL DATE	**DELIVERY MODE**
07/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/955,367	ATTIE ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,7 and 9-18* is/are pending in the application.

4a) Of the above claim(s) *4,7,9,10,14 and 16-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,11-13 and 15* is/are rejected.

7)☒ Claim(s) *1,5,11 and 12* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0407*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 30, 2007 has been entered.

2. Claims 1, 5, 11, and 12 have been amended and claims 13-18 have been added.

Election/Restrictions

3. Applicant is reminded that genes and combinations other than SREBP and a particular combination of genes including SREBP have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim (see, e.g., the Office action of April 8, 2004). Claims 4, 7, 9, and 10 remain withdrawn from consideration. Additionally, new claims 14 and 16-18 are withdrawn from consideration, as these new claims do not encompass SREBP or an elected combination including SREPB.

Accordingly, claims 1, 5, 11-13 and 15 are now under consideration. Regarding claims 1, 5, and 11-12, it is also noted that the claims as presently written no longer encompass, e.g., combinations including add1/SREBP and the other genes recited in the claims (but rather refer to other genes in the alternative only), and that the claims have been examined only to the extent that they are drawn to the elected invention.

Information Disclosure Statement

4. Regarding the information disclosure statement filed April 30, 2007, it is noted that the IDS fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the citation provided for the third item listed thereon ("Lee, Y.H., supplement") is incomplete. For example, the actual source of the information, publication date, etc. are not provided (and it is noted that the document itself does not appear to contain such information). Accordingly, this reference has been placed in the application file, but could not be considered by the examiner. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Objections

5. Claims 1, 5, and 11-12 are objected to because the claims encompass non-elected subject matter. In particular, the claims recite non-elected genes in the alternative (rather than as part of the elected gene combination), such that the claims encompass methods in which only non-elected genes are detected. Appropriate correction is required.

Declaration under 37 CFR 1.132

6. The Declaration under 37 CFR 1.132 filed April 30, 2007 is insufficient to overcome the rejection of claims 1, 5, and 11-12 based upon lack of enablement as set

forth in the last Office action. Because the Declaration is also pertinent to new claims 13 and 15, the discussion of the Declaration follows the rejections of claims 1, 5, 11-13 and 15 for lack of enablement set forth below.

Claim Rejections - 35 USC § 112, first paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 11-12 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of diagnosing obesity or susceptibility to obesity in a mouse comprising determining decreased expression in adipose tissue of SREBP, alone or in combination with cytochrome c oxidase subunit VIIIa and/or stearoyl-CoA desaturase, does not reasonably provide enablement for methods of diagnosing obesity or susceptibility to obesity in individuals other than mice, or for methods of diagnosis or prognosis of the "transition from obese" to diabetic in any type of individual. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level

of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (*MPEP* 2164.01(a)).

The elected invention of claim 11 is drawn to a method for "the diagnosis or prognosis of obesity, incipient obesity, or the transition from obese to diabetic" in an "individual" in which decreased expression of add1/SREBP in the adipose tissue of the individual as compared to "non-diabetic and non-obese individuals" indicates "susceptibility to obesity, incipient obesity, or the transition from obesity to diabetes." The elected invention of claim 12 is drawn to a method "of diagnosing susceptibility to obesity" in an individual in which decreased expression of add1/SREBP in the adipose tissue of the individual as compared to "a non-obese individual" indicates "susceptibility to obesity." Claim 15 is drawn to a method of diagnosing susceptibility to obesity" in an individual in which decreased expression of add1/SREBP in the adipose tissue of the individual as compared to "a non-obese individual" indicates that the individual is "susceptible to obesity." The specification teaches that SREBP, cytochrome c oxidase subunit VIIIa and stearoyl-CoA desaturase each exhibit decreased expression in multiple strains of obese mice (see Table 1 and the description thereof on page 4).

It is unpredictable as to whether one of skill in the relevant art could use applicant's invention in a manner reasonably commensurate with the instant claims. Because Applicant's disclosure provides evidence that SREBP, cytochrome c oxidase subunit VIIIa, and stearoyl-CoA desaturase each exhibit decreased expression in

adipose tissue of obese mice, one of skill in the art would reasonably consider decreased expression of SREBP, alone or in combination with these other 2 genes, in adipose tissue as one factor in diagnosing or determining susceptibility to obesity in mice. However, the specification does not includes these genes among those disclosed in Table 3 as being associated with hyperglycemia and diabetic disease. The specification states that a subset of genes "including the beta-3 adrenergic receptor, demonstrated changes in expression in both diabetes and obesity" (p. 4); however, none of SREBP, cytochrome c oxidase subunit VIIIa, or stearoyl-CoA desaturase are taught as being among this subset of genes. It is further noted that the specification itself teaches that "only 10% of individuals who are obese are diabetic" (p. 2); accordingly, the teachings of the specification indicate that a gene exhibiting modified expression in an obese individual might or might not exhibit a similar pattern of expression in a diabetic. Further, the specification does not provide evidence that determining the expression of any of these genes would allow one to determine a diagnosis for obesity, transition from obesity to diabetes, etc., in any type of individual, or a diagnosis of obesity in any individuals other than mice. For example, no data obtained in any other type of individual is included in the specification, nor does the specification establish that, e.g, any of the mouse strains employed are known to exhibit changes in expression patterns similar to those observed in, e.g., obese humans as compared to non-obese humans, etc. Further, the specification is only enabling with respect to comparisons made using adipose tissue; the specification is silent with regard to the use of tissue types other than adipose tissues, and thus does not establish

that valid comparisons of expression levels may be made using any other tissue type. Accordingly, the teachings of the specification alone are insufficient to enable the use of the invention as claimed. Lacking guidance from the specification, one of skill in the art may look to the teachings of the art for further guidance and enablement of a claimed invention. However, in the instant case, the prior art is silent with respect to an association between expression levels of SREBP, alone or in combination with cytochrome c oxidase subunit VIIIa and/or stearoyl-CoA desaturase, and obesity or the transition from obesity to diabetes. Given the high level of skill of one skilled in the relevant art, it is clearly within the ability of such an artisan to carry out further experimentation aimed at identifying such associations. However, the outcome of such further research cannot be predicted, and thus it is unknown as to whether any quantity of experimentation would be sufficient to enable the claimed invention. Thus, it would require undue experimentation to use applicant's invention in a manner reasonably commensurate with the instant claims.

9. Claims 1, 5, and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These

factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (*MPEP* 2164.01(a)).

The elected invention of claim 1 is drawn to a method for "the diagnosis of susceptibility to diabetes" in an "individual" in which decreased expression of add1/SREBP in the adipose tissue of the individual as compared to a "non-diabetic individual" indicates that the individual is "susceptible to diabetes." The elected invention of claim 5 is drawn to a method "for the diagnosis of predisposition to diabetes" in an individual in which decreased expression of add1/SREBP in the adipose tissue of the individual as compared to "non-diabetic individuals" indicates that the individual is "predisposed to diabetes." Claim 13 is drawn to a method of diagnosing susceptibility to diabetes" in an individual in which decreased expression of add1/SREBP in the adipose tissue of the individual as compared to "a non-diabetic individual" indicates that the individual is "susceptible to diabetes."

It is unpredictable as to whether one of skill in the relevant art could use applicant's invention. The specification teaches that SREBP, cytochrome c oxidase subunit VIIIa and stearoyl-CoA desaturase each exhibit decreased expression in multiple strains of obese mice (see Table 1 and the description thereof on page 4). However, the specification does not includes these genes among those disclosed in

Table 3 as being associated with hyperglycemia and diabetic disease. The specification states that a subset of genes "including the beta-3 adrenergic receptor, demonstrated changes in expression in both diabetes and obesity" (p. 4); however, none of SREBP, cytochrome c oxidase subunit VIIIa, or stearoyl-CoA desaturase are taught as being among this subset of genes. It is further noted that the specification itself teaches that "only 10% of individuals who are obese are diabetic" (p. 2); accordingly, the teachings of the specification indicate that a gene exhibiting modified expression in an obese individual might or might not exhibit a similar pattern of expression in a diabetic. It is also noted that the teachings of the specification are limited to mice and to samples of adipose tissue, while the claims encompass any type of "individual" and the use of any type of control sample (as opposed to, e.g., "adipose tissue" from a non-diabetic individual). Thus, the teachings of the specification alone are insufficient to enable the use of the invention. Lacking guidance from the specification, one of skill in the art may look to the teachings of the art for further guidance and enablement of a claimed invention. However, in the instant case, the prior art is silent with respect to an association between expression levels of SREBP, alone or in combination with cytochrome c oxidase subunit VIIIa and/or stearoyl-CoA desaturase, and diabetes. Given the high level of skill of one skilled in the relevant art, it is clearly within the ability of such an artisan to carry out further experimentation aimed at identifying such associations. However, the outcome of such further research cannot be predicted, and thus it is unknown as to whether any quantity of experimentation would be sufficient to

enable the claimed invention. Thus, it would require undue experimentation to use applicant's invention.

Response to arguments and Declaration under 37 CFR 1.132

10. It is first noted that Applicant's response and Declaration under 37 CFR 1.132 (hereinafter simply referred to as "the Declaration") have been considered to the extent that they are pertinent to the elected invention, which, as noted above, is drawn to methods involving SREBP and combinations including SREBP.

Applicant's response refers to and relies upon the Declaration, noting that it "is intended to establish that (1) the claimed methods apply equally to diagnosing disease in humans as well as mouse; (2) the specification as a whole along with the state of the art as of the filing date are sufficient to establish enablement for claimed methods; and (3) the genetic associations predicted by applicants have been validated independently."

With regard to the numerous references relied upon in both the response and the Declaration that were published subsequent to the filing of the instant application, it is again noted that it is the state of the art as of the filing date of an application that is used to determine whether the enablement requirement has been met (see MPEP 2164.05(a)). Thus, for example, the fact that later publications may demonstrate expression patterns in humans similar to those observed by applicants in mice does not establish that, at the time the instant invention was made, applicant's claims were enabled with regard to individuals other than mice. Rather, such later publications might establish enablement in humans as of the date the human data became available

(i.e., the publication date of the cited references), but not as of the date of filing of the instant application. None of these later-published references appear to provide evidence of, e.g., data supporting applicant's claims being disclosed prior to or on applicant's effective filing date.

Next, both the response and the Declaration argue that mice were widely used models of obesity and diabetes, as well as other diseases, at the time the invention was made. While this is acknowledged, applicants still have not established via evidence, references, etc., that the particular mice employed in the assays described in the specification were actually known to be reliable models having gene expression patterns predictive of expression patterns in humans, other mammals, etc. Further, both the response and the Declaration note the existence of particular types of transgenic mice that have "been produced that have similar protein expression profiles to humans" (see paragraph 4 of declaration); however, it does not appear that the mice of the specification are of this type, nor does the Declaration assert this. Thus, applicant's arguments with regard to the reliance on mouse expression data as predicting expression patterns in other types of individuals is not persuasive.

Finally, applicant's arguments in the response and the Declaration with regard to the existence of an association between SREPB expression and diabetes are simply inconsistent with the teachings set forth in the specification itself. As noted above, the specification clearly discloses different categories of genes, including some associated with obesity, some associated with diabetes, and some associated with both obesity and diabetes. The specification very clearly does not include SREBP in the disclosure

of genes associated with diabetes; rather, that gene is reported as having decreased expression in the adipose tissue of obese mice. One of skill in the art would not have concluded, based on the teachings of the specification and of the prior art, that SREBP expression was an indicator of diabetes or diabetes susceptibility. The fact that later, post-filing date publications may establish such an association cannot be relied upon to establish enablement as of applicant's filing date. Accordingly, the arguments of the response and of the Declaration are not persuasive.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1, 5, 11-13 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the selected gene." There is insufficient antecedent basis for this limitation in the claim.

Claim 5 is indefinite over the recitation of the limitation "determining the expression pattern of a gene.....the gene encoding add1/SREBP or cytochrome c oxidase subunit VIIa in the adipose tissue of the individual." It is not clear whether the recitation "in the adipose tissue of the individual" is merely intended to further limit a property of the recited genes (e.g., to specify a type of tissue where the genes may be expressed), or whether this recitation refers back to the "sample of adipose tissue"

previously referenced in the claim. Accordingly, the actual manipulations required to practice the claimed method are not clear.

Claim 5 recites the limitation "the selected gene." There is insufficient antecedent basis for this limitation in the claim.

Claim 11 recites the limitation "the selected gene." There is insufficient antecedent basis for this limitation in the claim.

Claim 11 is indefinite over the recitation of the limitations "a non-diabetic and non-obese individuals" and "non-obese and non-diabetic individuals." It is not clear whether these recitations encompass comparisons with, e.g., one or more non-obese individuals and one or more non-diabetic individuals, or whether the claim requires a comparison with one or more individuals who are both non-obese AND non-diabetic. Clarification is required.

Claim 12 recites the limitation "the selected gene." There is insufficient antecedent basis for this limitation in the claim.

Claim 13 recites the limitation "the non-diabetic individuals." There is insufficient antecedent basis for this limitation in the claim because the claim previously refers to only a single non-diabetic individual.

Claim 15 is indefinite because it is not clear how or whether the "comparing" and "diagnosing" steps relate to one another. In particular, it is noted that each of the steps refers to "a non-obese individual," such that the claim appears to encompass a method in which expression in multiple non-obese individuals is examined, and thus in which the "diagnosing" of the claim does not actually involve or require the "comparing" step.

This rejection could be overcome by amending the "diagnosing" step to refer to "the non-obese individual."

Conclusion

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday and Thursday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571/272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Diana B. Johannsen
Primary Examiner
Art Unit 1634